



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Ralph M. ELLISON et al.

Title: COMPOSITIONS AND METHODS FOR THE
TREATMENT OF PRIMARY AND METASTATIC
NEOPLASTIC DISEASES USING ARSENIC
COMPOUNDS

Appl. No.: 10/649,944

Filing Date: 08/28/2003

Examiner: Not yet assigned

Art Unit: 1614

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Mail Stop Amendment
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR §1.56. A copy of each listed document is being submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

RELEVANCE OF EACH DOCUMENT

Any document listed on the attached PTO/SB/08 was cited as being relevant during the prosecution of the corresponding European applications. A copy of each of the European Search Reports is attached setting forth the portion of each document considered relevant by the examiner. An English-language counterpart of the foreign-language documents has not been provided. The absence of a translation or an English-language counterpart document does not relieve the PTO from its duty to consider any submitted document (37 CFR §1.98 and MPEP§609).

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

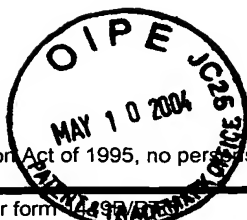
Respectfully submitted,

Date 10 May 2004

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5404
Facsimile: (202) 672-5399

By S. A. Bent

Stephen A. Bent
Attorney for Applicant
Registration No. 29,768



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | |
|--|--|-------------------------------|------------------|
| Substitute for form 10499/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: May 10, 2004 (use as many sheets as necessary) | | Complete if Known | |
| | | Application Number | 10/649,944 |
| Sheet 1 of 2 | | Filing Date | 08/28/2003 |
| | | First Named Inventor | Ralph M. ELLISON |
| | | Group Art Unit | 1614 |
| | | Examiner Name | Unassigned |
| | | Attorney Docket Number | 077319-0384 |

| U.S. PATENT DOCUMENTS | | | | | | |
|-----------------------|-----------------------|----------------------|-----------------------------------|---|--|---|
| Examiner Initials* | Cite No. ¹ | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number | Kind Code ² (if known) | | | |
| | | | | | | |

| FOREIGN PATENT DOCUMENTS | | | | | | | | |
|--------------------------|-----------------------|-------------------------|---------------------|--------------------------------------|--|---|---|----------------|
| Examiner Initials* | Cite No. ¹ | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Documents | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| | | Office ³ | Number ⁴ | Kind Code ⁵ (if known) | | | | |
| | | | FR 2 699 820 | | Eric PICHOT | 12/24/1992 | | |

| NON PATENT LITERATURE DOCUMENTS | | | |
|---------------------------------|-----------------------|--|----------------|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ |
| | | International Search Report | |
| | | Matthew BLOCK et al., "Biological Studies with Arsenic IV. The Histopathologic Effect of Arsenic Upon the Hematopoietic Tissues of Patients with Leukemia", The Journal of Laboratory and Clinical Medicine, Vol. 41, No. 4, 4/1953, pp. 499-515. | |
| | | P. ROUSSELOT et al., "Arsenic derivatives: Old drugs for new indications!, Les Derives Arsenicaux: De Vieux Medicaments Pour Des Indications Renouvelees", Hematologie, Vol. 4, no. 3, 5/1998, pp. 95-97. | |
| | | P. ROUSSELOT et al., "Arsenic trioxide (AS ₂ O ₃) and Melarsoprol induce myeloma cell apoptosis in vitro with a preferential effect on tumoral cells in patients' bone marrow", BLOOD, vol. 90, no. 10, 11/15/1997, page 325A. | |
| | | Z. XIE et al., "Melarsoprol and arsenic trioxide increase cell death on doxorubicin-resistant human leukemia and myeloma cells by regulating expression of BCL-2 apoptosis regulatory family", BLOOD, vol. 90, no. 10, 11/15/1997, pp. 495 A. | |
| | | DATABASE EPODOC 'Online! European Patent Office, the Hague, NL., CN1180563, 5/6/1998, Zhao QINGTUAN: XP002260136 *abstract*. | |
| | | International Search Report | |
| | | Edward B. SILBERSTEIN, "Radionuclide Therapy of Hematologic Disorders", Seminars in Nuclear Medicine, Vol. 9, No. 2, 4/1979, pp. 100-107. | |
| | | David A. SEARS MD, "History of the Treatment of Chronic Myelocytic Leukemia", American Journal of the Medical Sciences, Vol. 296, No. 2, 8/1988, pp. 85-86. | |

| | | | |
|--------------------|--|-----------------|--|
| Examiner Signature | | Date Considered | |
|--------------------|--|-----------------|--|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | | | |
|---|---|--------------------------|------------------|------------------------|-------------|
| Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: May 10, 2004 <i>(use as many sheets as necessary)</i> | | Complete if Known | | | |
| | | Application Number | 10/649,944 | | |
| | | Filing Date | 08/28/2003 | | |
| | | First Named Inventor | Ralph M. ELLISON | | |
| | | Group Art Unit | 1614 | | |
| | | Examiner Name | Unassigned | | |
| Sheet | 2 | of | 2 | Attorney Docket Number | 077319-0384 |

| NON PATENT LITERATURE DOCUMENTS | | | |
|---------------------------------|-----------------------|--|----------------|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issuè number(s), publisher, city and/or country where published. | T ⁶ |
| | | Zhi-Xiang SHEN et al., "Use of Arsenic Trioxide (As ₂ O ₃) in the Treatment of Acute Promyelocytic Leukemia (APL); II. Clinical Efficacy and Pharmacokinetics in Relapsed Patients", Blood, Vol. 89, No. 9, 5/1997, pp. 3354-3360. | |
| | | International Search Report | |
| | | W. ZHANG et al., "The induction of apoptosis and cell cycle arrest by arsenic trioxide in lymphoid neoplasms", Leukemia (1998), vol. 12, no. 9, 9/1998, pp. 1383-1391. | |
| | | John G. KIDD, "EFFECTS OF ARSENIC AZOPROTEINS ON MOUSE LYMPHOMA CELLS IN VIVO* With Observations on the Effects of Other "Anti-Lymphoma" Agents and On the Susceptibility to these Effects of Lymphoma Cells of Various Types", Journal of Experimental Medicine, vol. 108, 1958, pp. 665-684. | |
| | | Jacques DEBRAY, "Treatment of Hodgkin's Disease", Therapie, vol. 9, 1954, pp. 106-118. | |
| | | G. LOTTI, "Abandonment of arsenic in medical therapy of malignant granuloma (Hodgkin's disease): is it justified?!" Revue Medicale Du Moyen-Orient, vol. 24, no. 2, 3/1967 pp. 110-111. | |
| | | International Search Report | |
| | | S. ROSNER, "Immunological Enhancement of Chemotherapy in Advanced Brain Cancer", ACTA. NEUROL. LATINOAMER. Vol. 21, No. 4, 1975, pp. 126-132. | |
| | | S. SHIMOTSUURA, "STUDIES ON THE ANTINEOPLASMIC ACTIONS OF AS ₂ O ₃ " Shika Gakuho - Journal of Tokyo Dental College Society, vol. 86, no. 8, 1986, pp. 1237-1253. | |
| | | P. ZHANG et al., "Treatment of Acute Promyelocytic Leukemia with Intravenous Arsenic Trioxide" Zhonghua Xueyexue Zazhi - Chinese Journal of Hematology, vol. 17, no. 2, 2/1996, pp. 58-60. | |
| | | D.A. Sears, "History of the Treatment of Chronic Myelocytic Leukemia", American Journal of Medical Sciences, vol. 296, no. 2, 8/1988, pp. 85-86. | |
| | | Y.L. KWONG et al., "Delicious Poison: Arsenic Trioxide for the Treatment of Leukemia", Blood, vol. 89, no. 9, 5/1997, pp. 3487-3488 | |
| | | Edward B. SILBERSTEIN, "Radio nuclide Therapy of Hematologic Disorders", Seminars in Nuclear Medicine, vol. 9, no. 2, 4/1979, pp. 100-107. | |
| | | | |

| | | | |
|--------------------|--|-----------------|--|
| Examiner Signature | | Date Considered | |
|--------------------|--|-----------------|--|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.